Although the molecular load of pathologically occult pelvic lymph node metastases may indeed be a predictor of outcome in a univariate model, the extreme heterogeneity and verification bias inherent in this patient sample makes it difficult to ascertain whether it would be a predictor of outcome in multivariable models using other patient data sets.

These 2 articles suggest that assessment for the presence of occult lymph node metastasis in prostate cancer seems to be an exciting and powerful way to determine a patient's risk profile.

The era of molecular diagnostics and multiple predictive biomarkers in prostate cancer has arrived. These 2 articles suggest that assessment for the presence of occult lymph node metastasis in prostate cancer seems to be an exciting and powerful way to determine a patient's risk profile. Further systematic testing on tissue from patients treated elsewhere will help us elucidate whether these specific predictions made on these specific data sets can be generalized to risk stratification, and ultimately therapeutic guidance, of all patients undergoing treatment for prostate cancer. ■

References

1. Han M, Partin AW, Zahurak M, et al. Biochemical (prostate specific antigen) recurrence probability following radical prostatectomy for clinically localized prostate cancer. *J Urol.* 2003;169:517-523.
2. Khan MA, Partin AW, Mangold LA, et al. Probability of biochemical recurrence by analysis of pathologic stage, Gleason score, and margin status for localized prostate cancer. *Urology.* 2003;62:866-871.

Pediatric Urology

Dextranomer/Hyaluronic Acid Implantation for Vesicoureteral Reflux

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Elmore and colleagues from Atlanta recently reported their experience with new contralateral vesicoureteral reflux (NCVUR) after endoscopic treatment of reflux with dextranomer/hyaluronic acid (Dx/HA), and another study by this group evaluated success rates after an initial Dx/HA treatment failure.

New Contralateral Vesicoureteral Reflux Following Dextranomer/Hyaluronic Acid Implantation: Incidence and Identification of a High Risk Group

Elmore JM, Kirsch AJ, Lyles RH, et al.

J Urol. 2006;175:1097-1101.

The occurrence of NCVUR after open surgical ureteral reimplantation is as high as 20%. It is thought to be due to secondary intermittent reflux, destabilization of the contralateral ureter during mobilization of the refluxing ureter, or high detrusor pressure.[1] Elmore and colleagues examined 126 children who underwent unilateral Dx/HA for unilateral reflux. Approximately 40% of the patients were treated with Dx/HA injection as primary therapy and had only 1 preoperative voiding cystourethrogram (VCUG). Of the 17 children (13.5%) who developed NCVUR, 9 were grade I, 6 were grade II, and 2 were grade III. No variable independently seemed to be directly related to the incidence of NCVUR. Statistical analysis suggests that girls younger than 5 years more commonly developed NCVUR. Patients with a higher preoperative grade of reflux and those with fewer preoperative VCUGs, including those undergoing treatment as primary therapy, did not demonstrate an increased incidence. The investigators suggest assessing the contralateral ureter at the time of Dx/HA treatment, especially in girls aged less than 5 years, and they recommend prophylactic Dx/HA injection in select cases.

Dextranomer/Hyaluronic Acid for Vesicoureteral Reflux: Success Rates After Initial Treatment Failure

Elmore JM, Scherz HC, Kirsch AJ.

J Urol. 2006;175:712-715.

Parents often ask what is the next step if the first Dx/HA injection fails. Elmore and colleagues reviewed their experience with patients who fail initial treatment. Currently, Kirsch and colleagues[2] report a 92% success rate for patients undergoing Dx/HA implantation for grades I to IV VUR with a modified STING (subureteral transurethral injection) technique. Elmore and colleagues reported on a total of 42 children (mean age, 5 years) who underwent a second Dx/HA treatment. Follow-up was available in 39 patients (53 ureters) (14 patients had bilateral and 25 unilateral VUR). Before the second injection the mean grade of reflux was 2.2. After the second Dx/HA injection reflux resolved in 35 of 39 patients (90%) and 47 of 53 ureters (89%). When evaluated by VUR grade, reflux resolution occurred in 7 of 8 ureters (88%) with grade I, 24 of 26 (92%) with grade II, and 16 of 19 (84%) with grade III. The study is important because it

aids in the counseling of parents after initial treatment failure and demonstrates the high success rate of a second Dx/HA injection for the treatment of persistent VUR. ■

References

1. Elder JS. This month in pediatric urology. *J Urol.* 2006;175:807-808.
2. Kirsch AJ, Perez-Brayfield M, Smith EA, Scherz HC. The modified STING procedure to correct vesicoureteral reflux: improved results with submucosal implantation within the intramural ureter. *J Urol.* 2004;171:2413-2416.

Urinary Incontinence

Botulinum Toxin A in the Treatment of Neurogenic and Idiopathic Urinary Incontinence

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Anticholinergic therapy has long been considered the "gold standard" for treating urinary incontinence (UI) of both neurogenic and idiopathic origins. However, for those who fail this conservative measure for lack of efficacy or intolerable side effects, second-line treatments such as intradetrusor injections of botulinum toxin type A (BoNTA) have been studied. Initial studies have shown BoNTA to be of benefit clinically, as demonstrated by improvement in incontinence urodynamically as well as by quality-of-life (QOL) assessment.

A definitive explanation of how BoNTA exerts its effect on the overactive bladder is still unavailable. It does cause a reversible chemodenervation by inhibition of neuronal acetylcholine secretion but seems to have a different mechanism of action in smooth muscle than in skeletal muscle. Clinical data suggest that there are similar responses to BoNTA for patients with neurogenic and idiopathic causes of UI. However, more studies are needed to further delineate the optimal treatment regimen for both patient populations.

Botulinum Toxin in the Treatment of Neurogenic Bladder in Adults and Children

Schurch B, Schulte-Baukloh H.

Eur Urol Suppl. 2006;5:679-684.

This randomized clinical trial evaluated the effectiveness of focal injections of BoNTA in relieving symptoms of UI and reducing elevated detrusor pressures associated with the risk of renal complications as evaluated in both adults and children with neurogenic UI. Study 1 included 59 adults who received either placebo or BoNTA (200 U or 300 U BOTOX; Allergan, Irvine, CA) via 30 intradetrusor injections. Study 2 included 24 children with neurogenic UI at risk of kidney impairment who were given injections with BoNTA at 12 U/kg (maximum: 300 U) at approximately 40 sites in the detrusor.

In the first study, changes in UI frequency, urodynamic parameters including maximum detrusor pressure and maximum bladder capacity, and QOL were assessed throughout the 24 weeks following injection. Results showed that BoNTA at doses of 200 U and 300 U reduced the incidence of UI episodes by 50% and were associated with improvements in urodynamic parameters and QOL. There were no marked differences between the 2 BoNTA doses administered. However, the study was not powered to detect differences between the 2 doses. The efficacy was maintained for the 24-week duration of the study, suggesting that the duration of effect is greater than 6 months.

In the second study, cystometric measures and incontinence scores were assessed before and at 1, 3, and 6 months after BoNTA treatment in children who required regular clean intermittent catheterization (CIC) and were at a high risk of impaired kidney function. The incontinence score decreased at 1, 3, and 6 months by 46%, 15%, and 13%, respectively. Maximum detrusor pressure had decreased by 41% at 1 month and by 22% at 3 months (and had increased nonsignificantly by 4% at 6 months). Maximum bladder capacity had increased by 35%, 23%, and 36%, respectively. To assess the long-term success of repeated injections, data were also reviewed for 4 children who received at least 5 injections. There was no evidence of drug resistance, and bladder compliance was increased by 109% 6 months after the fifth injection.

These results suggest that BoNTA therapy may reduce the risk of vesicoureteric reflux and subsequent renal impairment and may also postpone or reduce the necessity for bladder augmentation surgery. Both studies add to the increasing evidence for the efficacy of BoNTA in the management of neurogenic UI in children and adults.

Efficacy of Botulinum Toxin A in the Treatment of Female Idiopathic Detrusor Overactivity Incontinence: Long-Term Results of a Prospective Nonrandomised Study

Werner M, Kuschel S, Schmid DM, Schuessler B.

Eur Urol Suppl. 2006;5:685-690.